

In re Application of:
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IN THE CLAIMS

Please cancel Claims 1, 7, 10, 12-14, and 22, without prejudice.

Please amend Claims 2-4, 8, 9, 11, 15, 16, and 19 and add new Claims 23-29, to replace the canceled Claims 1, 7, 10, 12-14, and 22, as shown below.

1 (Canceled).

2 (Currently amended). The compound of claim 23[[1]], wherein E₁, E₃, and E₄ are -O, and E₂ is -NH.

3 (Currently amended). The compound of claim 23[[1]], wherein R₁ and R₂ are -H, alkyl, or substituted alkyl, and R₃ is hydroxy or alkoxy.

4 (Currently amended). The compound of claim 23[[1]], wherein R₁ is substituted alkyl.

5 (Original). The compound of claim 4, wherein the substituted alkyl is a halogenated alkyl.

6 (Original). The compound of claim 5, wherein the halogenated alkyl is a chlorinated alkyl.

7 (Canceled)

8 (Currently amended). A pharmaceutical composition comprising at least one compound of claim 23[[1]] in a pharmaceutically acceptable carrier therefor.

9 (Currently amended). An article of manufacture comprising packaging material and a pharmaceutical composition contained within said packaging material, wherein said packaging material comprises a label which indicates that said pharmaceutical composition can be used for treatment of cell proliferative disorders and wherein said pharmaceutical composition comprises at least one compound of claim 23[[1]].

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10 (Canceled).

11 (Currently amended). The pharmaceutical composition of claim 25[[10]], further comprising at least one additional anti-neoplastic agent.

12-14 (Canceled).

15 (Currently amended). The method of claim 27[[13]], wherein the mammalian cell is human.

16 (Currently amended). The method of claim 27[[13]], wherein the disorder is characterized by the formation of neoplasms.

17 (Original). The method of claim 16, wherein the neoplasms are selected from mammary, small-cell lung, non-small-cell lung, colorectal, leukemia, melanoma, pancreatic adenocarcinoma, central nervous system (CNS), ovarian, prostate, sarccff of soft tissue or bone, head and neck, gastric which includes thyroid and non-Hodgkin's disease, stomach, myeloma, bladder, renal, neuroendocrine which includes thyroid and non-Hodgkin's disease and Hodgkin's disease neoplasms.

18 (Original). The method of claim 17, wherein the neoplasms are colorectal neoplasms.

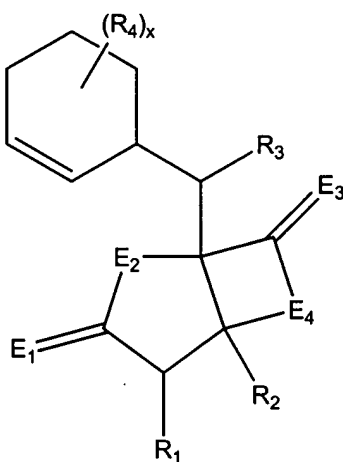
19 (Currently amended). A method for inhibiting proliferation of mammalian cells, comprising administering to a subject in need thereof a therapeutically effective amount of a compound of claim 23[[1]].

20 (Original). The method of claim 19, wherein the mammalian cells are human.

21 (Original). The method of claim 20, wherein the cells are selected from mammary, small-cell lung, non-small-cell lung, colorectal, leukemia, melanoma, pancreatic adenocarcinoma, central nervous system (CNS), ovarian, prostate, sarcoma of soft tissue or bone, head and neck, gastric, stomach, myeloma, bladder, renal, and neuroendocrine cells.

22 (Canceled).

23 (New). A compound having the structure (I):



(I)

wherein:

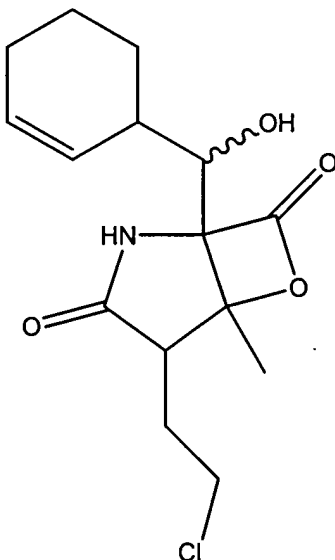
R₁ to R₃ are each independently -H, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, cycloalkyl, substituted cycloalkyl, alkoxy, substituted alkoxy, thioalkyl, substituted thioalkyl, hydroxy, halogen, amino, amido, carboxyl, -C(O)H, acyl, oxyacyl, carbamate, sulfonyl, sulfonamide, or sulfonyl,

each R_4 is independently alkyl, substituted alkyl, alkenyl,
substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl,
cycloalkyl, substituted cycloalkyl,

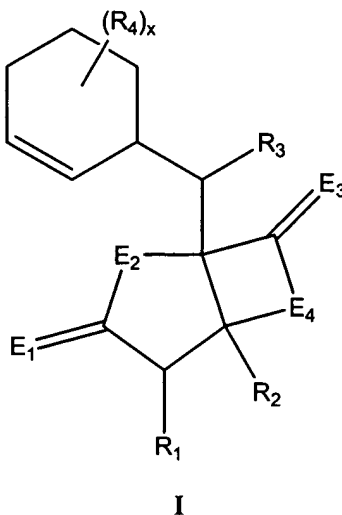
E_1 to E_4 are each independently $-O$, $-NR_5$, or $-S$, wherein R_5 is $-H$
or C_1 - C_6 alkyl, and

x is 0 to 8.

24 (New). A compound having the structure:



25 (New). A pharmaceutical composition useful for inhibiting proliferation of hyperproliferative mammalian cells, comprising an effective amount of a pharmaceutically acceptable carrier and a compound having the structure:



wherein:

R₁ to R₃ are each independently -H, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, cycloalkyl, substituted cycloalkyl, alkoxy, substituted alkoxy, thioalkyl, substituted thioalkyl, hydroxy, halogen, amino, amido, carboxyl, -C(O)H, acyl, oxyacyl, carbamate, sulfonyl, sulfonamide, or sulfonyl,

each R₄ is independently alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl,

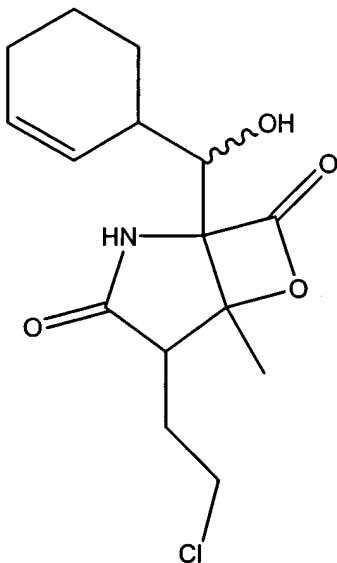
E₁ to E₄ are each independently -O, -NR₅, or -S, wherein R₅ is -H or C₁-C₆ alkyl, and

x is 0 to 8.

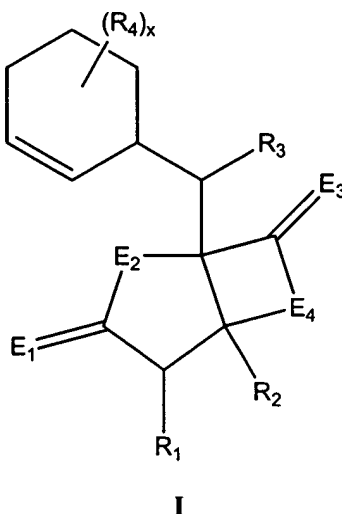
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26 (New). A pharmaceutical composition useful for inhibiting proliferation of hyperproliferative mammalian cells, comprising an effective amount of a pharmaceutically acceptable carrier and a compound having the structure:



27 (New). A method for treating a mammalian cell proliferative disorder, comprising administering to a subject in need thereof a therapeutically effective amount of a compound having the structure:



wherein:

R₁ to R₃ are each independently -H, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, cycloalkyl, substituted cycloalkyl, alkoxy, substituted alkoxy, thioalkyl, substituted thioalkyl, hydroxy, halogen, amino, amido, carboxyl, -C(O)H, acyl, oxyacyl, carbamate, sulfonyl, sulfonamide, or sulfonyl,

each R₄ is independently alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl,

E₁ to E₄ are each independently -O, -NR₅, or -S, wherein R₅ is -H or C₁-C₆ alkyl, and

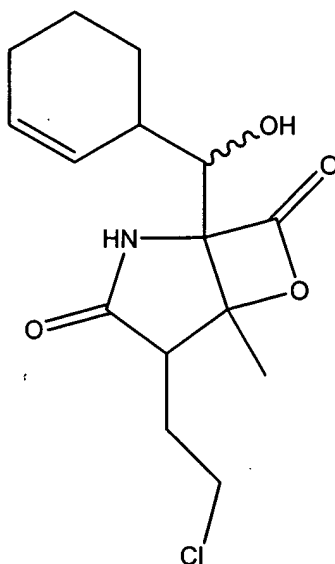
x is 0 to 8'

thereby treating a mammalian cell proliferative disorder.

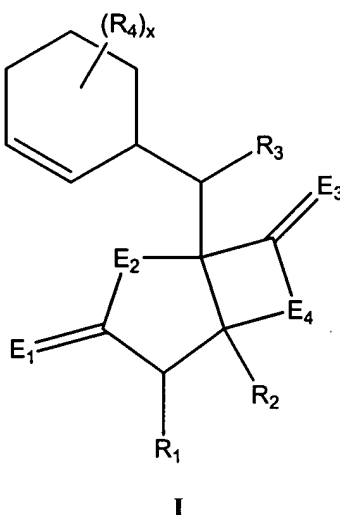
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28 (New). The method of claim 27, wherein the compound has the structure:



29. (New) A method for producing a compound having the ability to inhibit the proliferation of hyperproliferative mammalian cells, wherein said compound has structure (I):



wherein:

R₁ to R₃ are each independently -H, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, cycloalkyl, substituted cycloalkyl, alkoxy, substituted alkoxy, thioalkyl, substituted thioalkyl, hydroxy, halogen, amino, amido, carboxyl, -C(O)H, acyl, oxyacyl, carbamate, sulfonyl, sulfonamide, or sulfonyl,

each R₄ is independently alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl,

E₁ to E₄ are each independently -O, -NR₅, or -S, wherein R₅ is -H or C₁-C₆ alkyl, and

x is 0 to 8,

the method comprising:

- a) cultivating a culture of a *Salinospora* sp. strain CNB392 or CNB476;
- b) isolating from the culture at least one compound of structure (I).